## REMARKS/ARGUMENTS

The Examiner is requiring restriction to one of the following groups:

Group 1: Claims 1-15, 17-21, 24 and 25, drawn to double stranded oligonucleotides targeted to the  $\alpha$ ,  $\alpha'$  or  $\beta$  subunit of mouse CK2 protein kinase. Election of this invention requires a further election of a single nucleotide sequence as set forth below.

Group 2: Claims 1-15, 17-21, 24 and 25, drawn to double stranded oligonucleotides targeted to the  $\alpha$ ,  $\alpha'$  or  $\beta$  subunit of human CK2 protein kinase.

Election of this invention requires a further election of a single nucleotide sequence as set forth below.

Group 3: Claim 16, drawn to a transgenic nonhuman animal comprising the precursor of Claim 11 as it reads on mouse CK2 protein kinase.

Group 4: Claim 16 drawn to a transgenic nonhuman animal comprising the precursor of Claim 11 as it reads on human CK2 protein kinase.

Group 5: Claims 22-23, drawn to use of an oligonucleotide of Claims 1, 11 or 14 as they read on mouse CK2 protein kinase for preparing a medicinal product for use in prevention or treatment of cancer.

Group 6: Claims 22-23, drawn to use of an oligonucleotide of Claims 1, 11 or 14 as they read on human CK2 protein kinase for preparing a medicinal product for use in prevention or treatment of cancer.

Group 7: Claim 26, drawn to use of an oligonucleotide of claim 1 for screening for molecules capable of modulating the activity of the  $\alpha$ ,  $\alpha'$  or  $\beta$  subunit of mouse CK2 protein kinase.

Group 8: Claim 26, drawn to use of an oligonucleotide of Claim 1 for screening for molecules capable of modulating the activity of the  $\alpha$ ,  $\alpha'$  or  $\beta$  subunit of mouse CK2 protein kinase.

Applicants provisionally elect Group 2, Claims 1-15, 17-21, 24, and 25 drawn to double stranded oligonucleotides targeted to the  $\alpha$ ,  $\alpha'$  or  $\beta$  subunit of human CK2 protein kinase and further elect SEQ ID No: 26 as a single nucleotide sequence, with traverse on the grounds that no adequate reasons and/or examples have been provided to support a conclusion of patentable distinctiveness between the identified groups. Also, it has not been shown that a burden exists in searching the claims of the eight groups.

Moreover, the MPEP at § 803 states as follows:

"If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on its merits, even though it includes claims to distinct or independent inventions."

Applicants respectfully submit that a search of all of the claims would not impose a serious burden on the Office.

Finally, Applicants respectfully submit that the requirement of unity of invention is fulfilled since Groups 1 to 8 relate to claims that are so linked as to form a single inventive concept.

As regards unity of invention, the Examiner is of the opinion that the claims are directed to double-stranded oligonucleotides targeted to two different transcripts, respectively from a mouse CK2 protein kinase subunit and a human CK2 protein kinase subunit. Contrary to this opinion, the claims are directed to small interfering RNAs (siRNAs) targeted to a transcript of a CK2 protein kinase subunit of a mammal which includes a human and a mouse species.

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This is supported by the examples showing clearly that the claimed siRNAs target both the human and the murine sequences:  $siRNA CK2\beta15$  which comprises the sequence SEO ID No: 26 from the human CK2  $\beta$  subunit and inhibits murine CK2 protein kinase expression (examples 3 and 4 and figures 1 to 3). In addition, siRNAs CK2α3 and CK2α7, which comprise, respectively, the sequence SEQ ID No: 1 and the sequence SEQ ID No: 10 from the murine CK  $\alpha$  subunit, inhibit human CK2 protein kinase expression (example 5; figure 4).

Therefore, the special technical feature common to Groups 1 to 8 is a siRNA targeted to a transcript of a CK2 protein kinase subunit.

Furthermore, the alternatives as defined in Claim 1 are of similar nature since: (i) all of the alternatives are directed to siRNAs which belong to an art recognized class of compounds in the art to which the invention pertains, and (ii) all the alternatives have a common activity which is CK2 protein kinase expression inhibition by RNA interference.

The special technical feature common to Groups 1 to 8 is novel and not obvious in view of the prior art, for the following reasons:

## Novelty

Ulloa et al., (EMBO, 1993, 12, 1633-1640) discloses single-stranded antisens oligodeoxynucleotides which are different from siRNA (small double-stranded RNA molecules). In addition, the oligonucleotides of <u>Ulloa et al.</u> target the sequence from positions 97 to 116 of the murine CK2 protein kinase α subunit transcript or the sequence from positions 100 to 120 of the murine CK2 protein kinase  $\alpha$ ' subunit transcript which are different from the sequence targeted by the claimed siRNA.

## Non-obviousness

To inhibit CK2 protein expression, Ulloa et al. uses single-stranded antisens oligodeoxynucleotides which target positions 97 to 116 of the murine CK2 protein kinase  $\alpha$  Application No. 10/563,011

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subunit transcript or positions 100 to 120 of the murine CK2 protein kinase  $\alpha$ ' subunit

transcript.

Orlandini et al. (J. Biol. Chem., 1988, 273, 21291-21297) teaches only that the CK2

protein kinase  $\alpha$  subunit has oncogenic properties.

Elbashir et al. teaches only the mechanism of interference by siRNA.

Nothing in these documents suggest siRNA targeted to other positions of the CK2

protein kinase  $\alpha$ ,  $\alpha$ ' or  $\beta$  subunit transcripts.

For these reasons, the special technical feature common to Groups 1 to 8 is not

obvious in view of Ulloa et al., combined with Orlandini et al. and Elbashir et al.

Accordingly, and for the reasons presented above, Applicants submit that the Office

has failed to meet the burden necessary in order to sustain the Restriction Requirement.

Withdrawal of the Restriction Requirement is respectfully requested.

Applicants respectfully submit that the above-identified application is now in

condition for examination on the merits, and early notice of such action is earnestly solicited.

Respectfully submitted,

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